Assessment of trans-vaginal ultrasound guided aspiration of endometrioma in recurrence and IVF outcomes in infertile cases

Maryam Masoumi Shahrbabak¹, Victoria Habibzadeh², Faridadin Ebrahimi Meimand^{3*}, Sepideh Ebrahimi Meimand⁴

¹Obstetrics & gynecology Resident, Kerman university of Medical Sciences, Department of Obstetrics & Gynecology, Kerman, Iran. ²Assistant professor, Kerman University of Medical Sciences, Department of Obstetrics & Gynecology, Kerman, Iran. ³General surgeon, Kerman University of medical sciences, department of surgery, Kerman, Iran. ⁴Medical Student, Tehran University of medical sciences, Tehran, Iran.

Abstract

Background: One of the effective and less invasive treatments in patients with recurrent endometrioma with infertility can be trans-vaginal sonography guided aspiration and ethanol injection in cysts. Our goal is to assess the recurrence rate of endometrioma after this treatment and its effectiveness on intra vitro fertilization (IVF) outcomes in these cases. **Methods**: This study is a clinical trial. Cases were selected among patients at infertility center of "Afzali-pour" hospital, and classified into two groups. Trans-vaginal sonography guided aspiration and ethanol injection were performed in patients of the case group, but only aspiration of cysts was done in patients of the control group. After 3 months of aspiration, IVF was done for patients and then they were examined for the recurrence of endometrioma and results of IVF. **Results**: Average numbers of transferred fetuses were 2.63 ± 0.3 and 1.94 ± 0.2 in the case and control groups, respectively (p value= 0.019). Recurrent percentages of cyst formation in the case and control groups were 36.8% and 63.1%, respectively (p value = 0.105). The cyst size after aspiration averaged 0.71 ± 0.1 and 1.57 ± 0.2 cm in the case and control groups, respectively, which statistically had no significant difference. **Conclusion**: The number of the transferred fetuses in the case group was significantly more than the control group, which shows higher fertility in the former than in the latter. Besides, the recurrence of cyst formation and the size of new cysts were less in the case group but these parameters were not statistically significant.

Keywords: Endometrioma, Aspiration, Ethanol injection, Intra vitro fertilization

INTRODUCTION

Endometriosis is one of the common gynecological diseases in which the endometrial tissue (glandular epithelium) is found out of the uterus $^{[1, 2]}$. This disease afflicts 20%-40% of women who suffer from infertility $^{[3]}$, although it is also reported in 5%-10% of fertile women $^{[4, 5]}$.

Endometrioma also may damage the stroma of the ovary ^[6, 7], which leads to a decline both in ovarian reserve and available follicles in ovulation induction ^[8, 9].

In 1991, The simple aspiration of endometrioma directed by trans-vaginal sonography was suggested as an alternative treatment for patients who refused surgical treatment ^[10] and the study reported variable rates of recurrence after the aspiration ^[11, 12]. A combination of aspiration and ethanol injection directed by trans-vaginal sonography was suggested as another treatment to reduce surgical complications, with effective reduction of both cyst size and symptoms related to the pressure impact of the cyst in endometrioma ^[13-15].

In a study on 41 cases of endometrioma that failed in using IVF, transferring embryos and the fertility in each cycle had significant increases after the aspiration of endometrioma

directed by trans-vaginal sonography the count of oocytes [10].

Lee et al. (2014) examined the clinical outcomes of endometrioma (surgical treatment and ethanol injection directed by trans-vaginal sonography) and compared them with a control group (without treatment). The examination showed that antral follicle count, the retrievable oocyte counts, mature oocytes, and the fertile oocytes of those received the surgery were less than the other two groups, but

Address for correspondence: Faridadin Ebrahimi Meimand, General surgeon, Kerman University of medical sciences, department of surgery, Kerman, Iran. Email: ebrahimif63@gmail.com

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 3.0 License, which allows others to remix, tweak, and build upon the work non commercially, as long as the author is credited and the new creations are licensed under the identical terms.

How to cite this article: Masoumi Shahrbabak, M., Habibzadeh, V., Ebrahimi Meimand, F., Ebrahimi Meimand, S. Assessment of trans-Vaginal Ultrasound guided Aspiration of Endometrioma in recurrence and IVF outcomes in infertile cases. Arch Pharma Pract 2020;11(S4):80-4.

there were generally no significant differences among the

three groups in pregnancy rate for each cycle or for each transferring embryo, implantation of embryo, and miscarriage ^[16]. Tinkanen showed that small endometrioma did not reduce the success of IVF treatment ^[17]. Yazbeck showed that ovarian response declined during IVF-ET cycles in patients with a history of severe endometriosis and laparoscopic excision of endometriomas compared to women with mild or minimal endometriosis without ovarian surgery ^[18]. Chang states "ultrasound-guided sclerotherapy with 95% ethanol retention is an effective alternative therapy for recurrent ovarian endometrioma, in particular in selected patient groups" ^[19]. It seems that ultrasound guided aspiration of endometrioma can be an effective and safe alternative therapeutic procedure in infertile patients with endometrioma to improve their reproductive outcomes ^[20]. Mussi showed that transvaginal ultrasound-guided endometrioma aspiration might determine tissue trauma that could enhance adhesion formation ^[21]. In addition, Yazbeck showed that ovarian response decreased during IVF-ET cycles in patients with a history of severe endometriosis ^[18].

The increasing prevalence of endometrioma in societies has an impact on infertility, and each surgical treatment in endometrioma leads to a decline in the ovarian reserve and an increase in the risk of adhesion. Therefore, the current study aims to evaluate the effectiveness of aspiration and ethanol injection directed by trans-vaginal sonography as a less invasive and more economical method than surgery to treat patients with recurred endometrioma after the surgery. This trial also evaluates recurrence rate after using this treatment and its effectiveness in the success of other assisted reproductive methods.

MATERIALS AND METHODS

The current study is a randomized clinical trial. Cases were selected among patients at the clinical center of "Afzali-pour" hospital between March 2015 and March 2016. This study was approved by the Committee of Ethics, Kerman Research Center.

Selected patients met the following criteria

- 1. Cases were 20-45 years old
- 2. BMI of the cases were 18-29 kg/m2
- 3. Cases were under infertility treatment and were candidates of IVF
- 4. Patients had a history of cystectomy for endometrioma
- 5. Cyst size was at least 3 cm.

Exclusion criteria were:

- 1. Solid pattern, disordered cyst wall, thick septations, and other suspicious findings for malignancy
- 2. Location of endometrioma cysts far from vaginal septum and poor accessibility to remove them.
- 3. A positive past medical history of heart, renal or liver diseases
- 4. Male factor infertility

Diagnosis of endometrioma was based on sonography findings or pathology of a previous surgery. Patients included in the research were classified into two groups. Trans-vaginal sonography guided aspiration and ethanol injection were done in patients of the case group, but only aspiration of cysts was performed in those of the control group.

In the operation room, patients were sedated and then aspiration of the endometrioma cysts was directed under the guidance of trans-vaginal sonography using ovarian puncture needles.

After aspiration, internal space of the cyst was washed by normal saline and 95% ethanol was injected (maximum volume of injection was 100 CC) according to the aspirated liquid volume of the cyst. After three months of this procedure, IVF was done for the patients.

In the control group in which the inclusion criteria were similar to the case group, the cyst aspiration was done by sonography similarly to the case group, but the ethanol injection was not done and the variables were examined the same as the case group.

A questionnaire of basic information was filled by asking the patients and using their medical profile. This questionnaire contained demographic information, years of infertility, date of the first diagnosis of endometrioma, and symptoms and former surgeries. After doing the medical procedure, later follow-ups were recorded in their profile. The outcomes were examined and then analyzed by SPSS software.

FINDINGS

A number of 19 patients in each group entered the study.

The average ages were 28.3 ± 3.5 and 31.4 ± 5.5 years in the case and the control groups, respectively. The age of husband in the case and control groups averaged 30.4 ± 4.5 and 32.3 ± 3.4 years, respectively. All the examined patients were nullipara. There were four cases that had a history of abortion and one case with ectopic pregnancy in the case group. The average menarche ages were 12.9 ± 1.5 and 14.2 ± 1.2 years in the case and control groups, respectively. Other information of the patients' symptoms is summarized in Table 1.

Table1.symptoms	Baseline patie	nt character	ristics and
Variables	Positive/negative	Case group	Control group
Regular mense	Positive	13 (68.4%)	16 (76.3%)
	negative	6 (31.6%)	3 (23.7%)
Dyspareunia	positive	10 (52.6%)	4 (22.2%)
	negative	9 (47.4)	15 (77.8%)
Pelvic pain	positive	6 (31.6%)	3 (17.6%)

Masoumi Shahrbabak et al.: Assessment of trans-Vaginal Ultrasound guided Aspiration of Endometrioma in recurrence and IVF outcomes in infertile cases

	negative	13 (68.4%)	14 (82.4%)
Dysmenorrhea	positive	17 (89.5%)	10 (52.6%)
	negative	2 (10.5%)	9 (47.4%)
Abortion	Primary	13 (68.4%)	17 (89.4%)
Infertility type	secondary	2 (10.5%)	2 (10.5%)
	both	4 (21%)	0 (0%)
Positive B-HCG	positive	3 (17.3%)	16 (82.4%)
	Negative	4 (21.1%)	15 (78.9%)

Table 2 represents the outcomes of IVF, including number of retrieved follicles and oocytes, number of fetuses, and size of cysts before and after the aspiration, in both case and control groups. There were no significant differences between the two groups, except for the number of transferred fetuses in the case (4.74) and control (2.89) groups (p-value = 0.019).

Table 2. IVF outcomes					
Variable	Case group	Control group	P value		
Follicle number	8.35	9.84	0.142		
Oocyte count	7.16	5.53	0.1		
Fetus number	4.74	2.89	0.019		
Size of the cyst before treatment	4.18 cm	4.63 cm	0.259		
Average size of the cyst 3 months after the aspiration	0.1 cm ±0.71	0.2 cm ±1.57	0.210		

Recurrence rate of cyst formation after the treatment in the case group (36.8%) was less than the control group (63.1%). In the examined groups, there were no significant differences statically (p value = 0.105)



Figure 1. Rate of cyst recurrence in the experimental groups

The average volume of injected ethanol in case group was 43.14 cc. This amount has a direct average significant

relation with the size of cyst after treatment and an average inverse relation with the cyst recurrence rate.

Table 3. The relation of ethanol volume with the sizeand recurrence of cyst in the case group					
Variable	Pearson correlation coefficient	P value			
Cyst size	0.549	0.015			
Cyst recurrence	0.561-	0.012			

DISCUSSION AND CONCLUSION

The frequencies of positive B-HCG, oocyte count, follicle count, and cyst size had no significant differences in the examined patients of case and control groups. Although the averages of cyst size after aspiration were 0.71 ± 0.1 and 1.57 ± 0.2 cm in the case and control groups, respectively, which statistically had no significant difference. However, the cyst size of the case group was less than the control group after the treatment, which may show better effectiveness.

The frequency of the embryo count in the examined patients of the case group was significantly more than that of the control group, which shows higher fertility in the former than in the latter.

Unlike the current study, in a study on 41 endometrioma cases who failed in IVF, the oocyte, transferred fetuses, and the fertility rate in each cycle had significant differences after the aspiration of endometrioma directed by transvaginal sonography ^[10].

Similar to the current study, Troiano et al. studied the effectiveness of aspiration of endometrioma directed by transvaginal sonography, and reported recurrence rates of 16.1 % and 66.6% after the aspiration of benign ovarian cysts and for endometrioma, respectively ^[22].

In another study, researchers examined the aspiration and injection of ethanol in the ovarian endometrioma and the effectiveness of receiving GNRH before and after aspiration and compared results using laparoscopy treatment. As with the current study, the recurrence rate and successful pregnancy rates were found to be higher in the aspiration of endometrioma directed by transvaginal sonography than the laparoscopy method ^[23].

Our observations are also in line with another study in 2003, in which researchers studied 24 marked cases of endometriosis and observed that the aspiration of edometrioma directed by transvaginal sonography was a better method to treat endometriosis ^[24].

Unlike the present study, a study showed that the recurrence rate was high (83.3%) after the aspiration of endometrioma directed by transvaginal sonography in the cases who had recurrence with the previous treatments, and all recurrence cases were early to happen only after 3 months of aspiration ^[25].

Contrary to our findings, Pabucca et al. investigated on 41 cases of ovarian endometrioma treated with aspiration, 40 cases of endometrioma without aspiration, 44 cases of endometrioma by surgical treatment, and 46 infertility cases by tubal factors. They detected that the aspiration of endometrioma before the induction neither increased the level of gonadotropins nor the number of follicles over 17 mm, oocytes in metaphase 2, the implantation rate, and finally the fertility. Besides, the aspiration of small endometrioma (1-6 cm) was not significantly beneficial in IVF and ICSI consequences ^[26].

Consistent with the current study, a study in 2008 showed that aspiration of endometrioma directed by transvaginal sonography and (ethanol 95%) injection were practical treatments and ethanol retention could lead to more decrease in the chance of recurrence of endometrioma relative to injection; however, there were no differences in antral follicle count, pain, and levels of CA-125 between two groups ^[27].

Unlike the current study, Lee et al. (2014) examined the effectiveness of the treatment of endometrioma by surgery or aspiration directed by transvaginal sonography and ethanol injection in comparison to a control group (without treatment). The study showed that total count of antral follicles, retrieved oocytes, and mature oocytes were lower in those who had surgery than other two groups, but there were no significant differences in pregnancy rate for each cycle or for each transferred embryo, implantation of embryo, and abortion rate ^[16].

Conclusion

Results of the current study showed that frequencies of positive B-HCG, oocyte, follicle count, and cyst size in the examined patients of the case group had no significant differences with the control group. However, the average cyst sizes after the aspiration were 0.71 ± 0.1 and 1.57 ± 0.2 in the case and control groups, respectively, which were not significantly different. On the other hand, the cyst size of the case group was less than that of the control group, which can show better treatment in the former.

Moreover, the frequency of fetus count in the case group was significantly more than the control group, which shows a higher fertility rate in the former than in the latter.

Recommendations

It is recommended to carry out a study with a larger sample size to compare this treatment with other surgical and medical treatments.

REFERENCES

- Ozkan S, Murk W, Arici A. Endometriosis and infertility: epidemiology and evidence-based treatments. Annals of the New York Academy of Sciences. 2008;1127:92-100.
- Opoien HK, Fedorcsak P, Omland AK, Abyholm T, Bjercke S, Ertzeid G, et al. In vitro fertilization is a successful treatment in endometriosis-associated infertility. Fertility and sterility. 2012;97(4):912-8.

- Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. Journal of Assisted Reproduction and Genetics. 2010;27(8):441-7.
- 4. Hart R. Unexplained infertility, endometriosis, and fibroids. BMJ: British Medical Journal. 2003;327(7417):721.
- Tamura H, Kishi H, Kitade M, Asai-Sato M, Tanaka A, Murakami T, et al. Clinical outcomes of infertility treatment for women with adenomyosis in Japan. Reproductive Medicine and Biology. 2017;16(3):276-82.
- Brosens I, Puttemans P, Gordts S, Campo R, Gordts S, Benagiano G. Early stage management of ovarian endometrioma to prevent infertility. Facts, Views & Vision in ObGyn. 2013;5(4):309-14.
- 7. Grandi G, Toss A, Cortesi L, Botticelli L, Volpe A, Cagnacci A. The association between endometriomas and ovarian cancer: preventive effect of inhibiting ovulation and menstruation during reproductive life. BioMed research international. 2015 Jan 1;2015.
- Matsuzaki S, Schubert B. Oxidative stress status in normal ovarian cortex surrounding ovarian endometriosis. Fertility and sterility. 2010;93(7):2431-2.
- 9. Garcia-Velasco JA, Somigliana E. Management of endometriomas in women requiring IVF: to touch or not to touch. Human Reproduction. 2009;24(3):496-501.
- Dicker D, Goldman JA, Feldberg D, Ashkenazi J, Levy T. Transvaginal ultrasonic needle-guided aspiration of endometriotic cysts before ovulation induction for in vitro fertilization. Journal of Assisted Reproduction and Genetics. 1991;8(5):286-9.
- Hsieh C-L, Shiau C-S, Lo L-M, Chang M-Y. Effectiveness of ultrasound-guided aspiration and sclerotherapy with 95% ethanol for treatment of recurrent ovarian endometriomas. Fertility and sterility. 2009;91(6):2709-13.
- 12. Zhu W, Tan Z, Fu Z, Li X, Chen X, Zhou Y. Repeat transvaginal ultrasound-guided aspiration of ovarian endometrioma in infertile women with endometriosis. American journal of obstetrics and gynecology. 2011;204(1):61.e1-6.
- Berlanda N, Vercellini P, Fedele L. The outcomes of repeat surgery for recurrent symptomatic endometriosis. Current Opinion in Obstetrics and Gynecology. 2010;22(4):320-5.
- Akamatsu N, Hirai T, Masaoka H, Sekiba K, Fujita T. Ultrasonically guided puncture of endometrial cysts--aspiration of contents and infusion of ethanol. Nihon Sanka Fujinka Gakkai Zasshi. 1988;40(2):187-91.
- Aflatoonian A, Rahmani E, Rahsepar M. Assessing the efficacy of aspiration and ethanol injection in recurrent endometrioma before IVF cycle: A randomized clinical trial. Iranian Journal of Reproductive Medicine. 2013;11(3):179-84.
- Lee K-H, Kim C-H, Lee Y-J, Kim S-H, Chae H-D, Kang B-M. Surgical resection or aspiration with ethanol sclerotherapy of endometrioma before in vitro fertilization in infertilie women with endometrioma. Obstetrics & gynecology science. 2014;57(4):297-303.
- 17. Tinkanen H, Kujansuu E. In vitro fertilization in patients with ovarian endometriomas. Acta obstetricia et gynecologica Scandinavica. 2000;79(2):119-22.
- Yazbeck C, Madelenat P, Sifer C, Hazout A, Poncelet C. [Ovarian endometriomas: Effect of laparoscopic cystectomy on ovarian response in IVF-ET cycles]. Gynecologie, obstetrique & fertilite. 2006;34(9):808-12.
- Chang MY, Hsieh CL, Shiau CS, Hsieh TT, Chiang RD, Chan CH. Ultrasound-guided aspiration and ethanol sclerotherapy (EST) for treatment of cyst recurrence in patients after previous endometriosis surgery: analysis of influencing factors using a decision tree. Journal of minimally invasive gynecology. 2013;20(5):595-603.
- Mittal S, Kumar S, Kumar A, Verma A. Ultrasound guided aspiration of endometrioma--a new therapeutic modality to improve reproductive outcome. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 1999;65(1):17-23.
- Muzii L, Marana R, Caruana P, Catalano GF, Mancuso S. Laparoscopic findings after transvaginal ultrasound-guided aspiration of ovarian endometriomas. Human reproduction (Oxford, England). 1995;10(11):2902-3.
- 22. Troiano R, Taylor K. Sonographically guided therapeutic aspiration of benign-appearing ovarian cysts and endometriomas. AJR American journal of roentgenology. 1998;171(6):1601-5.

- Noma J, Yoshida N. Efficacy of ethanol sclerotherapy for ovarian endometriomas. International Journal of Gynecology & Obstetrics. 2001;72(1):35-9.
- Acién P, Quereda FJ, Gómez-Torres M-J, Bermejo R, Gutierrez M. GnRH analogues, transvaginal ultrasound-guided drainage and intracystic injection of recombinant interleukin-2 in the treatment of endometriosis. Gynecologic and obstetric investigation. 2003;55(2):96-104.
- 25. Chan LY, So WW, Lao TT. Rapid recurrence of endometrioma after transvaginal ultrasound-guided aspiration. European Journal of

Obstetrics & Gynecology and Reproductive Biology. 2003;109(2):196-8.

- Pabuccu R, Onalan G, Goktolga U, Kucuk T, Orhon E, Ceyhan T. Aspiration of ovarian endometriomas before intracytoplasmic sperm injection. Fertility and sterility. 2004;82(3):705-11.
- Mgaloblishvili I, Mgaloblishvili M, Beriia N, Tabutsadze K. Transvaginal hydrolaparoscopy: treatment of ovarian endometriomaspreliminary identification of their dislocation by method of aspiration drainage. Georgian medical news. 2006(139):30-3.